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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,046	HALAZONETIS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/11/05; 05/17/05; 06/17/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,6,21,23,43-49,51-58 and 60-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,43-49,51-58 and 60-65* is/are rejected.

7)☒ Claim(s) *2,3,5 and 6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/11/05 has been entered.

Applicant cancels claims 50, 59 and adds new claims 60-66.

Since applicant has elected Group I, a nucleic acid of a mitotic checkpoint gene, chfr, for action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claim 66 directed to a method for detecting the sensitivity of tumor cells to killing by an agent that disrupts microtubule function have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03. Newly submitted claim 66 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The originally claimed invention and the invention of claim 66 do not relate to a single general

inventive concept because their same or corresponding technical feature is not a contribution over the prior art. The reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length of group 1 is known in the art, as shown by the pending 102 rejection (see 102 rejection below). Thus group 1 lacks novelty or inventive step, and does not make a contribution over the prior art.

Accordingly, claims 2-3, 5-6, 21, 23, 43-49, 51-58, 60-65 are being examined.

The following are the remaining rejections.

OBJECTION

In the specification:

The specification is objected to because Trademark names are not capitalized, for example, "taxol" recited on pages 42, 45.

In the claims:

Claim 58 is objected to, because claim 58 is currently amended, but it seems that by typographic error, claim 58 is labeled as "new".

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

1) Claims 21, 23, 43-49, 51-58, 60-65 are indefinite for the use of the language "specifically hybridizes" in claims 21, 49 and 60. Specific hybridization conditions are not defined by the claim (which reads on the full range of specific hybridization conditions, that is from very low specificity to very high specificity). Further, the specification does not provide a standard for ascertaining the requisite degree of

specific hybridization conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

2) Claim 47 recites the limitation "said subject" in claim 21. There is insufficient antecedent basis for this limitation in the claim 21, to which claim 47 is dependent.

Claim 56 recites the limitation "said mammal" in claim 49. There is insufficient antecedent basis for this limitation in the claim 49, to which claim 56 is dependent.

Claims 57-58 recites the limitation "said subject" in claim 49. There is insufficient antecedent basis for this limitation in the claim 49, to which claims 57-58 are dependent.

3) Claim 65 is indefinite, because it seems that by typographic error, claim 65 is dependent on claim 65.

For the purpose of compact prosecution, it is assumed that claim 65 is dependent on claim 62.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

1. Claims 57-58 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of "reduced expression" of a nucleotide sequence encoding Chfr polypeptide SEQ ID NO:2, claimed in Claims 57-58, has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for: 1) a method for assessing the sensitivity of a tumor cell to an agent which disrupt microtubule function, comprising examining the "substantial absence" of a chfr gene (claim 42), 2) a decrease in the number of colony-forming unit of DLD1-neo cells that express the neo selectable marker, but "do not express" the chfr sequence of SEQ ID NO:1, in response to the mitotic stress induced by Nocodazole or Taxol, a drug affecting microtubule dynamics (p.45,lines 6-10, p.40, line 1 and lines 21-23, p.42, lines 21-22), and 3) If Chfr is "inactivated" in human cancer, then its inactivation may underlie the increased sensitivity of cancer cells to antimitotic drugs (p.45, lines 21-22).

There is however no mention of "reduced expression" of a nucleotide sequence encoding Chfr polypeptide SEQ ID NO:2 in cancer cells that are sensitive to an agent that disrupts microtubule function.

The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.

2. Claims 60-65 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of "a nucleic acid sequence of between 12 to 50 nucleic acids in length" claimed in Claim 60 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for a range of 14 to 50 nucleotides in length, or 12 to 30 nucleotides in length (p.17, last paragraph, bridging p.18). There is however no mention of "a nucleic acid sequence of between 12 to 50 nucleic acids in length".

The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.

3. Claim 65 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of amplification of "nucleotides 180-399, 557-1128, 1516-2013" of SEQ ID NO:1 claimed in Claim 65 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for amplification of nucleotides 66-562, 352-1055, 771-1376, 904-1753, 904-1772, 904-1902, 1187-1753, 1187-1772, 1215-1753, 1215-1772, 1214-1902, and 1625-2279 of SEQ ID NO: 1 (table 1 on page 38).

There is however no mention of a composition for amplification of nucleotides 180-399, 557-1128, 1516-2013 of SEQ ID NO:1.

The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 21, 23, 44-49, 51-58, 60-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification lacks a clear written description of: 1) a nucleic acid fragment of between 12 to 30 or 12 to 50 nucleic acid in length that "specifically hybridizes" to a nucleic acid fragment of the same length from SEQ ID NO:1, or from the complete complement of SEQ ID NO:1, and 2) a "complementary strand" of a nucleotide sequence encoding SEQ ID NO:2.

Claims 21, 23, 44-49, 51-58, 60-65 are drawn to:

1) A reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length that "specifically hybridizes" to a nucleic acid fragment of the same length from SEQ ID NO:1, or the complete complement of said fragment (claims 21, 23, 43-48).

2) A kit comprising a nucleotide sequence that is between 12 to 30 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 nucleic acid fragment of SEQ ID NO:1, and a nucleotide sequence that is between 12 to 30 or 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 nucleic acid fragment of the complete complement SEQ ID NO:1 (claims 49, 51-58).

3) A composition comprising a pair of primers, said primer sequences consisting of a nucleotide sequence of between 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 50 nucleic acid fragment of a nucleotide sequence encoding SEQ ID NO:2, and a nucleotide sequence of between 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 50 nucleic acid fragment of the

"complementary strand" of a nucleotide sequence encoding SEQ ID NO:2 (claims 60-65).

It is noted that in view of a lack of a definition of "specific hybridizes", "specific hybridizes" encompasses a full range of specific hybridization conditions, from very low specificity to very high specificity, wherein under very low specificity, one would expect that the full length of unrelated sequences, of between 12 to 30 or 12 to 50 nucleotides in length, would attach to or hybridize to SEQ ID NO:1. In other words, the claimed hybridizing nucleic acid fragments are of unknown structure, and would hybridize to a nucleic acid fragment of the same length of SEQ ID NO:1.

Further, "a complementary strand" of a nucleotide sequence encoding SEQ ID NO:2 encompasses a full length or partial complementary strand of a nucleotide sequence encoding SEQ ID NO:2, wherein a partial complementary strand would share only a few nucleotides with a nucleotide sequence encoding SEQ ID NO:2.

The specification does not meet the written description requirement. The example of Lilly is clearly applicable to the instant application, because no representative number of species of the claimed hybridizing fragments under low specific hybridization conditions, or of the claimed complementary strand is disclosed, or known in the art, and no common structure among the claimed sequences is disclosed, or known in the art.

Further, the specification does not meet the written description requirement in view of the example of Enzo, because the specification does not disclose of sufficiently detailed, "relevant identifying characteristics, functional characteristics when coupled

with a known or disclosed correlation between function and structure, or some combination of such characteristics."

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

1. Claims 21, 23, 44-49, 51-58, 60-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a reagent consisting of a nucleic acid fragment of SEQ ID NO:1, consisting of between 12 to 30 nucleotides in length, or 2) a kit or a composition comprising a pair of primer sequences, consisting of a nucleic acid fragment of SEQ ID NO:1, consisting of between 12 to 30, or between 14 to 50 nucleotides in length, and a complete full length complement of a nucleic acid fragment of SEQ ID NO:1, consisting of between 12 to 30, or between 14 to 50 nucleotides in length does not reasonably provide enablement for 1) a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length that "specifically hybridizes" to a nucleic acid fragment of the same length from SEQ ID NO:1, or the complete complement of said fragment, or 2) a kit or a composition comprising a nucleotide sequence that is between 12 to 30 or 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 or 12 to 50 nucleic acid fragment of SEQ ID NO:1 or of a nucleotide sequence encoding SEQ ID NO:2, respectively, and a nucleotide sequence that is between 12 to 30 or 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 or 12 to 50 nucleic acid fragment of the complete complement SEQ ID NO:1 or the complementary strand of a nucleotide sequence encoding SEQ ID NO:2, respectively. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 21, 23, 44-49, 51-58, 60-65 are drawn to:

1) A reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length that "specifically hybridizes" to a nucleic acid fragment of the same length from SEQ ID NO:1, or the complete complement of said fragment (claims 21, 23, 43-48).

2) A kit comprising a nucleotide sequence that is between 12 to 30 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 nucleic acid fragment of SEQ ID NO:1, and a nucleotide sequence that is between 12 to 30 nucleotides in length, and that "specifically hybridizes' to a 12 to 30 nucleic acid fragment of the complete complement SEQ ID NO:1 (claims 49, 51-58).

3) A composition comprising a pair of primers, said primer sequences consisting of a nucleotide sequence of between 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 50 nucleic acid fragment of a nucleotide sequence encoding SEQ ID NO:2, and a nucleotide sequence of between 12 to 50 nucleotides in length, and that "specifically hybridizes' to a 12 to 50 nucleic acid fragment of the "complementary strand" of a nucleotide sequence encoding SEQ ID NO:2 (claims 60-65).

It is noted that in view of a lack of a definition of "specific hybridizes", "specific hybridizes" encompasses a full range of specific hybridization conditions, from very low specificity to very high specificity, wherein under very low specificity, one would expect

that the full length of unrelated sequences, of between 12 to 30 or 12 to 50 nucleotides in length, would attach to or hybridize to SEQ ID NO:1. In other words, the claimed hybridizing nucleic acid fragments are of unknown structure, and would hybridize to a nucleic acid fragment of the same length of SEQ ID NO:1.

Further, "a complementary strand" of a nucleotide sequence encoding SEQ ID NO:2 encompasses a full length or partial complementary strand of a nucleotide sequence encoding SEQ ID NO:2, wherein a partial complementary strand would share only a few nucleotides with a nucleotide sequence encoding SEQ ID NO:2.

Since the claimed fragments or primers would not necessarily be structurally related to SEQ ID NO:1, one would not expect that the claimed fragments or primers would be specific for SEQ ID NO:1 or amplify a portion of SEQ ID NO:1, and thus one would not know how to use the claimed invention.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

2. If Applicant could overcome the above 112, first paragraph, Claims 47-48, 57-58 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reagent or a kit useful for detecting expression of SEQ ID NO:1, does not reasonably provide enablement for a reagent or a kit useful in a PCR assay to detect the sensitivity to killing of tumor cells in a subject to an agent that disrupts microtubules function, wherein detection of reduced or absent expression of a nucleotide sequence encoding Chfr polypeptide SEQ ID NO:2 is indicative of said sensitivity. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 47-48, 57-58 are drawn to a reagent or a kit useful in a PCR assay to detect the sensitivity to killing of tumor cells in a subject to an agent that disrupts microtubules function, wherein detection of reduced or absent expression of a nucleotide sequence encoding Chfr polypeptide SEQ ID NO:2 is indicative of said sensitivity.

The specification discloses that Chfr check point is evident in primary human cells but is inactivated in four out of eight human "cancer cell lines" (p.45, lines 12-13). The specification discloses that one of the cancer cell line, U2OS has a mutation that inactivates the function of Chfr (p.40, last paragraph, bridging p.41). The specification discloses a decrease in the number of colony-forming unit of DLD1-neo cells that express the neo selectable marker, but do not express the chfr sequence of SEQ ID NO:1, in response to the mitotic stress induced by Nocodazole or Taxol, a drug affecting microtubule dynamics (p.45, lines 6-10, p.40, line 1 and lines 21-23, p.42, lines 21-22). The specification contemplates that "if" Chfr is inactivated in human cancer, then its inactivation may underlie the increased sensitivity of cancer cells to antimitotic drugs (p.45, lines 21-22).

One cannot extrapolate the teaching in the specification to the scope of the claims, because it is unpredictable that primary human cancer tissues would have inactivation of expression of SEQ ID NO:1, and therefore, it is unpredictable that the

claimed fragments of SEQ ID NO:1 would be useful for detecting the sensitivity to killing of tumor cells in a subject to an agent that disrupts microtubules function.

Although some human cancer cell lines have inactivation of expression of SEQ ID NO:1, one cannot extrapolate the expression of SEQ ID NO:1 in cancer cell lines to the expression of SEQ ID NO:1 in primary cancer tissues, because characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor, due to cell culture artifacts. Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded and that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the *bona fide* cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al (Immunol Ser, 1984, 23:181-207) specifically teaches that in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines and specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new artifactural antigens can occur as a result of culture (see attached abstract). Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). The evidence presented clearly demonstrates that in cell

culture systems, in general, and in cancer derived cell lines in particular, that artifactural chromosome constitutions and antigen expression are expected and must be taken into account when interpreting data received from cell line assays. Thus, based on the cell culture data presented in the specification, one cannot predict that expression of SEQ ID NO:1 is inactivated or absent in primary cancer tissues, nor one can predict that mutation of SEQ ID NO:1 that inactivates the function of SEQ ID NO:1 occurs in primary cancer tissues.

Further, the claims as written however encompasses a kit useful for detecting the sensitivity to killing of tumor cells, wherein said killing is a direct effect of taxol on any tumor cells, and wherein the reduced or absent expression of SEQ ID NO:1 could be the result of exposure to taxol, rather than a kit useful for detecting the sensitivity to mitotic stress induced by taxol.

However, it is noted that taxol, an agent that disrupts microtubule function, induces mitotic stress, and that said mitotic stress decreases survival of cancer cell lines that do not express SEQ ID NO:1, but not cell lines that express normal level of SEQ ID NO:1 (specification, p.42, last two paragraph, p.44 last two paragraphs, bridging p.45). There is no indication that taxol could kill any tumor cells, nor that the reduced or absent expression of SEQ ID NO:1 could be the result of exposure to taxol.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102(b or e)

1. Rejection under 35 USC 102(b) of claims 21, 47-48 pertaining to anticipation by JP06303997-A, 1994, GenBank Accession No:AAQ75652 remains for reasons already of record in paper of 02/11/05.

Applicant argues that the art sequence is a polyA sequence, not a coding sequence, and that the amendment of claim 21 requires the nucleotide sequence to be a fragment of the coding sequence of SEQ ID NO:1.

Applicant's arguments set forth in paper of 05/11/05 have been considered but are not deemed to be persuasive for the following reasons:

Applicant argues limitation not in the claims.

2. Claims 21, 44 remain rejected under 35 USC 102(e) as being anticipated by US 5,610054-A, GenBank Accession No:I57653, for reasons already of record in paper of 02/11/05.

Applicant argues that only a portion of the art sequence (13 nucleotides in length) hybridizes specifically to fragments (15 nucleotides in length) of the antisense sequence of SEQ ID NO:1.

Applicant's arguments set forth in paper of 05/11/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that "specifically hybridizes" encompasses hybridization under low specificity hybridization conditions.

Under low specific conditions of hybridization and wash, the entire length of the art sequence (15 nucleotides in length) would attach to or hybridize to the antisense sequence of SEQ ID NO:1.

3. Claims 21, 45 are rejected under 35 USC 102(b) as being anticipated by Gold, DP et al, 1993, GenBank Accession No:S86452, for reasons already of record in paper of 02/11/05.

Applicant argues that only a portion of the art sequence (14 nucleotides in length) hybridizes specifically to fragments (30 nucleotides in length) of the antisense sequence of SEQ ID NO:1.

Applicant's arguments set forth in paper of 05/11/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that "specifically hybridizes" encompasses hybridization under low specificity hybridization conditions.

Under low specific conditions of hybridization and wash, the entire length of the art sequence (30 nucleotides in length) would attach to or hybridize to the antisense sequence of SEQ ID NO:1.

4. Claims 21, 46 are rejected under 35 USC 102(b) as being anticipated by George JF et al, 1992, GenBank Accession No:S81367, for reasons already of record in paper of 02/11/05.

Applicant argues that only a portion of the art sequence (14 nucleotides in length) hybridizes specifically to fragments (27 nucleotides in length) of the antisense sequence of SEQ ID NO:1.

Applicant's arguments set forth in paper of 05/11/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that "specifically hybridizes" encompasses hybridization under low specificity hybridization conditions.

Under low specific conditions of hybridization and wash, the entire length of the art sequence (27 nucleotides in length) would attach to or hybridize to the antisense sequence of SEQ ID NO:1.

REJECTION UNDER 35 USC 103 (a), NEW REJECTION

Claims 23, 43 are rejected under 35 USC 103(a) as being obvious over US 5,610054-A, Gold, DP et al, or George JF et al, supra, in view of US 5,324,630, for reasons already of record in paper of 02/11/05.

Claim 23, 43 are drawn to a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that specifically hybridizes to a nucleic acid fragment of the same length from SEQ ID NO:1, or the complete complement of said fragment, wherein said reagent further comprising a detectable label, which could be a fluorescent label or an enzyme.

The teaching of US 5,610054-A, Gold, DP et al, or George JF et al has been set forth in previous Office action.

US 5,610054-A, Gold, DP et al, or George JF et al, however, does not teach a detectable label, which could be a fluorescent label or an enzyme.

US 5,324,630 teaches a diagnostic kit comprising a labeled nucleic acid probe in a container, and instruction for the detection method (claim 3). US 5,324,630 teaches that suitable labels could be enzymes, fluorescers (column 8, lines 13-16). US

5,324,630 teaches that polymerase chain reaction technique may be used for the production of the probe and/or amplification of the polynucleotides for synthetic purpose (column 4, lines 28-31).

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to label the sequence taught by US 5,610054-A, Gold, DP et al, or George JF et al with suitable labels such as enzymes, fluorescers taught by US 5,324,630, for use in the diagnosis of expression of the gene taught by US 5,610054-A, Gold, DP et al, or George JF et al, with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

July 15, 2005

SUSAN UNGAR, PH.D
PRIMARY EXAMINER